as said antibody or functional fragment comprising SEQ ID NOS:2 and 4.

REMARKS

Claims 1-6, 47 and 48 are pending in the above-identified application. Claims 1 and 6 have been amended above. Support for the amendments can be found in the specification including, for example, on page 8, lines 1-16; page 15, line 19 through page 16, line 2; page 16, lines 10-21; page 21, lines 3-5; page 22, line 22, through page 23, line 7, and page 28, lines 9-14. Accordingly, the amendments do not introduce new matter and entry thereof is respectfully requested. A marked-up copy of the amended claims is attached hereto as Appendix A.

Applicant would like to thank Examiner Helms for extending a personal interview with Applicant and Applicant's representatives on December 17, 2002. During the interview the rejections under 35 U.S.C. § 112, first paragraph were discussed. The subject matter discussed in the interview is set forth below.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 5 remains rejected under 35 U.S.C. § 112, first paragraph as lacking enablement allegedly because the data supporting enablement is based on *in vitro* cell culture whereas the claim, being directed to a pharmaceutical composition, reads on *in vivo* treatment for cancer. The Office Action alleges that one cannot extrapolate the teachings of *in vitro* experimental

data to *in vivo* activity. In this regard, the Office Action asserts that "petri dish cancer" is a poor representation of malignancy because cells in culture have different characteristics than human disease and further asserts that anticancer drug discovery is highly unpredictable. References to Freshney et al., Dermer et al., Gura et al. and Jain et al. are relied on in support of this rejection.

As discussed in the Examiner interview, Applicants have set forth in their previous Responses that therapeutic enablement is not required for the claimed subject matter. Claim 5 is a composition claim directed to a human monoclonal antibody or functional fragment and a pharmaceutical carrier. The claim does not recite and, therefore, is not limited to a method of *in vivo* administration for purposes of treating cancer. As such, any use that would reasonably correlate with the scope of the claim is sufficient to preclude a rejection for nonenablement based on how to use. MPEP § 2164.01(c), fourth paragraph.

Applicants have previously set forth multiple uses sufficient to support the full scope of the rejected claim. For example, the specification teaches administration to reduce the proliferation or viability of neoplastic cells (see page 28, lines 15-17, and page 30, lines 8-12) or to detect neoplastic cells (see page 28, lines 12-18). Accordingly, Applicants maintain that claim 5 is sufficiently enabled.

Moreover, and as discussed in the Examiner interview, the use of antibodies as therapeutics is well established in the

art. The specification describes throughout, and Applicants' previous Responses point out, that it is sufficient for an antibody to exhibit binding activity to a neoplastic cell in order for it to be beneficial for the treatment of a neoplastic disease. Applicants have additionally supplied extrinsic evidence to establish that antibodies are well accepted in the art for the treatment of a variety of diseases. As such, the assertion that cell-based assays fail to enable the claimed invention is unsupported as applied to antibody-based pharmaceutical compositions. Moreover, the assertion that anticancer drug discovery is unpredictable is non-analogous to the claimed invention because such art is directed to the screening of drug compounds and not based on antigen-antibody binding characteristics.

Briefly, in the Response filed February 20, 2001, Applicants submitted as Exhibit D a publication by Walsh, Nature Biotech. 18:831-833 (2000), which lists 18 monoclonal antibody-based products that have been approved for medical use in the United States or in the European Union. Because the Exhibits appeared to be missing from the Office's file, and for the Examiner's convenience, a complete copy of the Response and its exhibits are attached hereto as Exhibit 1.

As described in Walsh (Exhibit D), the treatment of cancer with an antibody-based pharmaceutical composition is a developed art having achieved both commercial and medical success. For example, Walsh describes on page 832, column 3, lines 27-29, that 31 monoclonal antibody-based products are in

clinical trials for cancer. Furthermore, Table 1 of Walsh lists 18 monoclonal antibody-based products that have been approved for medical use. Of these products at least four have been approved for cancer therapy including, OncoScint CR/OV for the treatment of colorectal and ovarian cancers, Rituxan for the treatment of non-Hodgkin's lymphoma, Herceptin for the treatment of metastatic breast cancer, and Mabthera for the treatment of non-Hodgkin's lymphoma. This level of success in the clinic contradicts the assertion in the Office Action that the use of antibodies to treat cancer is unpredictable or undeveloped. Absent evidence to the contrary, the assertion that pharmaceutical compositions comprising antibodies are not useful for cancer is unfounded. Accordingly, Applicants respectfully request that this ground of rejection be removed.

Claims 1-4 and 47-48 stand newly rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement allegedly for a human monoclonal antibody or antigen binding fragment thereof having any conservative substitutions in SEQ ID NOS: 2 and 4 that binds any neoplastic cell or antigen thereof.

Applicants contend that the claims are sufficiently enabled because the functional requirement to binding a neoplastic cell or antigen thereof merely ensures that a claimed antibody or functional fragment having a conservative substitution substantially maintains its original binding activity. However, Applicants have amended claim 1 above to recite that an antibody or functional fragment thereof having a conservative substitution of an amino acid binds the same

neoplastic cell or antigen thereof as the antibody or functional fragment comprising SEQ ID NOS:2 and 4. Therefore, the amendment clarifies that applicants are not claiming conservative substitutions that bind to any neoplastic cell or to any neoplastic antigen. Accordingly, this ground of rejection is rendered moot by the amendment and is respectfully requested to be withdrawn.

CONCLUSION

In light of the Amendments and Remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call Cathryn Campbell or the undersigned agent.

Respectfully submitted,

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APPENDIX A

1. (Amended) A human monoclonal antibody or functional fragment thereof, comprising the amino acid sequence of SEQ ID NO:2, or having a conservative substitution of an amino acid thereof, and the amino acid sequence of SEQ ID NO:4, or having a conservative substitution of an amino acid thereof, wherein said antibody or functional fragment thereof binds a neoplastic cell or antigen thereof[.] and wherein said antibody or functional fragment thereof having a conservative substitution of an amino acid binds the same neoplastic cell or antigen thereof as said antibody or functional fragment comprising SEQ ID NOS:2 and 4.